I. General Information:
   A. Definition: A chronic centralized pain sensitivity syndrome, characterized by diffuse, multifocal, migratory, waxing and waning pain, primarily described as arthralgia (joint pain) and myalgia (muscle pain)
   B. Prevalence: 2-8% of the population
   C. Gender distribution: criteria-dependant
      • 9:1 female to male ratio (1990 ACR criteria)
      • 2:1 female to male ratio (2010 ACR criteria)
   D. Age: childhood to elderly; largest prevalence between 25-60 years
   E. Risk factors:
      • Female gender
      • Family history, especially first-degree relativity (odds ratio, 8.5)
      • Twin concordance rate up to 50%
      • History of rheumatic disorders: osteoarthritis, rheumatoid arthritis, Lupus…etc.
      • “Pain-prone” phenotype
      • Prolonged stressors (physiological, psychological, social, emotional…etc.)
      • Trauma
      • Surgery
      • Certain preceding infections (EBV, Lyme, influenza, parasites…etc.) and exposures

II. Pathophysiology:
   A. Central sensitization: the dysregulation of the thalamus-hypothalamus-amygdala leading to pain and sensory processing abnormalities, which in turn leads to pain signal generation, pain amplification, decline in pain tolerance, hyperalgesia, allodynia, and global sensory hyperresponsiveness
      • Dysregulation of thalamus → pain and global sensory processing abnormalities
      • Dysregulation of hypothalamus → fatigue and temperature dysregulation
      • Dysregulation of amygdala → mood disturbances
   B. Central sensitization is characterized by significant derangements:
      • Increase of pain-provoking transmitters (glutamate, substance P, TNF-α, IL-1…etc.)
      • Decrease of relief transmitters (norepinephrine, epinephrine, dopamine, and serotonin)
      • Upregulation and plasticity of nociceptive neurons
      • Upregulation of limbic system and midbrain
      • Downregulation of frontal lobe (executive function)
   C. Central sensitization is multifactorial in etiology:

Multifactorial Etiology of Central Sensitization

(over)
III. Signs and Symptoms:

The Mohabbat Circle of Central Sensitization

- Cognitive changes/“brain fog”
- Arthralgia
- Myalgia
- Dizziness/light-headedness
- Temperature dysregulation
- Sleep disorder (T/L)
- Anxiety
- Fatigue
- TMJ dysfunction
- Postural orthostatic
- Urinary incontinence
- Irritable bowel symptoms
- Cognitive changes/“brain fog”
- Global sensory hyperresponsiveness

Central Sensitization

- Headaches (tension, migraines)
- Fatigue
- Food/milk allergy
- Depression
- Paresthesia
- Menstrual change/pelvic pain
- Photosensitivity
- Dizziness/light-headedness
- Generalized weakness
- Temperature dysregulation

IV. Diagnosis:

A. 1990 American College of Rheumatology Criteria:
   - Symptoms of widespread pain, occurring both above and below the waist and affecting both right and left sides of the body
   - Presence of at least 11 of 18 tender points

B. 2010 American College of Rheumatology Criteria:
   - Widespread pain index (WPI) ≥ 7 (out of 19) and Symptom Severity (SS) scale score ≥ 5 (out of 12) or WPI 3 - 6 and SS scale score ≥ 9
   - Symptoms present for at least 3 months
   - Symptoms not due to another underlying cause

C. Common Exclusionary Testing:
   - Complete blood count (CBC)
   - Electrolytes (including Calcium)
   - Liver and renal function tests
   - Thyroid-stimulating hormone
   - Morning cortisol
   - Fasting glucose
   - Inflammatory markers (ESR and CRP)
   - Anti-nuclear antibody
   - Rheumatoid factor/CCP
   - Vitamin D
   - Overnight oximetry

V. Management: requires a multifaceted approach

A. Medication management
   1. FDA-approved options:
      - Duloxetine (SNRI)
      - Milnacipran (SNRI)
      - Pregabalin (Alpha-2-delta calcium channel ligand)

2. Non-FDA-approved options
   - Tricyclic antidepressants
   - Selective serotonin reuptake inhibitors
   - Gabapentin
   - Non-steroidal anti-inflammatories
   - Acetaminophen
   - Muscle relaxants

B. Non-medication management
   - Ongoing patient education
   - Graded exercise
   - Dietary/weight modifications
   - Physical therapy
   - Occupational therapy
   - Cognitive behavioral therapy
   - Biofeedback therapy
   - Sleep hygiene

C. Opioids should be avoided due to their lack of benefit in fibromyalgia, propensity to lead to opioid-induced hyperalgesia, abuse/addiction/dependance potential, and side effect profile.

VI. References: